

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of P. Isakson et al.
Serial No. TBA
Filed HEREWITH
Confirmation No. TBA

Art Unit TBA

For TREATMENT OF INFLAMMATION AND INFLAMMATION-RELATED DISORDERS
WITH A COMBINATION OF A CYCLOOXYGENASE-2 INHIBITORS AND A
LEUKOTRIENE B₄ RECEPTOR ANTAGONIST
Examiner TBA

January 3, 2002

PRELIMINARY AMENDMENT A

Prior to calculating the filing fee in this matter, please enter the following amendments in the above-referenced application.

IN THE RELATED CASE:

Please replace the paragraph on Page 1, lines 7-8 with the following:

--This is a continuation of US Application Serial No. 08/661,641, filed June 11, 1996 which application is a continuation-in-part of US Application Serial No. 08/489,415, filed June 12, 1995.--

IN THE SPECIFICATION:

Please replace the paragraph on page 5, lines 6-12 with the following:

--In addition, the invention describes a combination comprising a therapeutically-effective amount of a leukotriene B₄ receptor antagonist and a cyclooxygenase-2 inhibitor selected from Taisho NS-398 (Methanesulfonamide, N-[2-(cyclohexyloxy)-4-nitrophenyl]), meloxicam (2H-1,2-Benzothiazine-3-carboxamide, 4-hydroxy-2-methyl-N-(5-methyl-2-thiazolyl)-, 1,1-dioxide), flosulide (Methanesulfonamide, N-[6-(2,4-difluorophenoxy)-2,3-dihydro-1-oxo-1H-inden-5-yl]), Merck MK-966 (2(5H)-Furanone, 4-[4-

(methylsulfonyl)phenyl]-3-phenyl), Merck L-752,860 and compounds of Formula I--

Please replace the paragraph beginning on page 8, line 26 and ending on page 9, line 5 with the following:

--Preferred leukotriene B₄ receptor antagonists include Bayer Bay-x-1005 ((R)-a-Cyclopentyl-4-(2-quinolinylmethoxy) benzene acetic acid), Ciba-Geigy CGS-25019C (Benzamide, 4-[[5-[4-(aminoiminomethyl)phenoxy]pentyl]oxy]-3-methoxy-N,N-bis(1-methylethyl)-, (2Z)-2-butenedioate), ebselen (1,2-Benzisoselenazol-3(2H)-one, 2-phenyl), Leo Denmark ETH-615 (Benzoic acid, 4-[[[(3-fluorophenyl)methyl][4-(2-quinolinylmethoxy)phenyl]amino]methyl]), Lilly LY-293111 (Benzoic acid, 2-[3-[3-[(5-ethyl-4'-fluoro-2-hydroxy[1,1'-biphenyl]-4-yl)oxy]propoxy]-2-propylphenoxy]), Ono ONO-4057 (Benzenepropanoic acid, 2-(4-carboxybutoxy)-6-[[5E)-6-(4-methoxyphenyl)-5-hexenyl]oxy]), Terumo TMK-688 (Carbonic acid, 4-[5-[2-[4-(diphenylmethoxy)-1-piperidinyl]ethyl]amino]-5-oxo-1,3-pentadienyl]-2-methoxyphenyl ethyl ester), Boehringer Ingleheim BI-RM-270 (2-Benzoxazoline, N-[(1S)-2-cyclohexyl-1-(2-pyridinyl)ethyl]-5-methyl), Lilly LY 213024 (Benzenepropanoic acid, 5-(3-carboxybenzoyl)-2-(decyloxy)), Lilly LY 264086 (9H-Xanthene-4-propanoic acid, 7-carboxy-3-(decyloxy)-9-oxo), Lilly LY 292728, Ono ONO LB457 (Benzenepropanoic acid, 2-(4-carboxybutoxy)-6-[[5E)-6-(4-methoxyphenyl)-5-hexenyl]oxy]), Pfizer 105696, Perdue Frederick PF 10042 (Pyrrolidine, 1-[5-hydroxy-5-[8-(1-hydroxy-2-phenylethyl)-2-dibenzofuranyl]-1-oxopentyl]), Rhone-Poulenc Rorer RP 66153 (2-Thiopheneheptanoic acid, .alpha.,.alpha.-dimethyl-3-(3-phenylpropyl)), SmithKline Beecham SB-201146 (2-Propenoic acid, 3-[6-[[3-aminophenyl)sulfinyl]methyl]-3-[[8-(4-methoxyphenyl)octyl]oxy]-2-pyridinyl]-, (2E)), SmithKline Beecham SB-201993 (Benzoic acid, 3-[[[6-[(1E)-2-carboxyethenyl]-5-[[8-(4-methoxyphenyl)octyl]oxy]-2-pyridinyl]methyl]thio]methyl]), Searle SC-53228 (2H-1-Benzopyran-2-propanoic acid, 7-[3-[2-(cyclopropylmethyl)-3-methoxy-4-

[(methylamino)carbonyl]phenoxy]propoxy]-3,4-dihydro-8-propyl-,
(2S)), Sumitamo SM 15178 (.beta.-Alanine, N-[[6-[(4-acetyl-2-
ethyl-5-hydroxyphenoxy)methyl]-2-pyridinyl]carbonyl]-N-ethyl),
American Home Products WAY 121006 ([1,1'-Biphenyl]-4-acetic acid,
2-fluoro-4'-(2-quinolinylmethoxy)), Bayer Bay-o-8276, calcitriol
(9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol,
(1.alpha.,3.beta.,5Z,7E)), Warner-Lambert CI-987 (2,4-
Thiazolidinedione,5-[[3,5-bis(1,1-dimethylethyl)-4-
hydroxyphenyl]methylene]), Merck and Co. L-651392 (3H-
Phenothiazin-3-one, 4-bromo-2,7-dimethoxy), Lilly LY 210073,
Lilly LY 223982 (Benzenepropanoic acid, 5-(3-carboxybenzoyl)-2-
[[[(5E)-6-(4-methoxyphenyl)-5-hexenyl]oxy]), Lilly LY-233569 (2-
Propenamide, N-hydroxy-N-methyl-3-[2-(methylthio)phenyl]), Lilly
LY-255283 (Ethanone, 1-[5-ethyl-2-hydroxy-4-[[6-methyl-6-(1H-
tetrazol-5-yl)heptyl]oxy]phenyl]), Merck and Co. MK-591 (1H-
Indole-2-propanoic acid, 1-[(4-chlorophenyl)methyl]-3-[(1,1-
dimethylethyl)thio]-a,a-dimethyl-5-(2-quinolinylmethoxy)-, sodium
salt), Merck and CO. MK-886 (1H-indole-2-propanoic acid, 1-[(4-
chlorophenyl)methyl]-3-[(1,1-dimethylethyl)thio]-a,a-dimethyl-5-
(1-methylethyl)), Ono ONO-LB-448, Purdue Frederick PF-5901
(Benzenemethanol, a-pentyl-3-(2-quinolinylmethoxy)), Rhone-
Poulenc Rorer RG 14893 (2-Naphthalenecarboxylic acid, 4-[2-
[methyl(2-phenylethyl)amino]-2-oxoethyl]-8-(phenylmethoxy)),
Rhone-Poulenc Rorer RP 66364, Rhone-Poulenc Rorer RP 69698
(Pyridine, 2-[[5-methyl-5-(1H-tetrazol-5-yl)hexyl]oxy]-4,6-
diphenyl), Searle SC-41930 (2H-1-Benzopyran-2-carboxylic acid, 7-
[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-
propyl), Searle SC-50505, Searle SC-51146, SmithKline Beecham
SK&F-104493 (5H-Pyrrolo[1,2-a]imidazole, 6,7-dihydro-2-(4-
methoxyphenyl)-3-(4-pyridinyl)), and Teinjin TEI-1338 (Benzoic
acid, 2-[[4-[2-[2-(2-naphthalenyl)ethenyl]cyclopropyl]-1-
oxobutyl]amino]-, methyl ester, [1R-[1.alpha.,2.beta.(E)]])--

Please replace the paragraph on page 9, lines 6-15 with the following:

--More preferred leukotriene B₄ receptor antagonists include Bayer Bay-x-1005 ((R)-a-Cyclopentyl-4-(2-quinolinylmethoxy)benzeneacetic acid), Ciba-Geigy CGS-25019C (Benzamide, 4-[[5-[4-(aminoiminomethyl)phenoxy]pentyl]oxy]-3-methoxy-N,N-bis(1-methylethyl)-, (2Z)-2-butenedioate), ebselen (1,2-Benzisoselenazol-3(2H)-one, 2-phenyl), Leo Denmark ETH-615 (Benzoic acid, 4-[[[(3-fluorophenyl)methyl][4-(2-quinolinylmethoxy)phenyl]amino]methyl]), Lilly LY-293111 (Benzoic acid, 2-[3-[3-[(5-ethyl-4'-fluoro-2-hydroxy[1,1'-biphenyl]-4-yl)oxy]propoxy]-2-propylphenoxy]), Ono ONO-4057 (Benzenepropanoic acid, 2-(4-carboxybutoxy)-6-[[[(5E)-6-(4-methoxyphenyl)-5-hexenyl]oxy]), Terumo TMK-688 (Carbonic acid, 4-[5-[[2-[4-(diphenylmethoxy)-1-piperidinyl]ethyl]amino]-5-oxo-1,3-pentadienyl]-2-methoxyphenyl ethyl ester), Boehringer Ingleheim BI-RM-270 (2-Benzoxazolamine, N-[(1S)-2-cyclohexyl-1-(2-pyridinyl)ethyl]-5-methyl), Lilly LY 213024 (Benzenepropanoic acid, 5-(3-carboxybenzoyl)-2-(decyloxy)), Lilly LY 264086 (9H-Xanthene-4-propanoic acid, 7-carboxy-3-(decyloxy)-9-oxo), Lilly LY 292728, Ono ONO LB457 (Benzenepropanoic acid, 2-(4-carboxybutoxy)-6-[[[(5E)-6-(4-methoxyphenyl)-5-hexenyl]oxy]), Pfizer 105696, Perdue Frederick PF 10042 (Pyrrolidine, 1-[5-hydroxy-5-[8-(1-hydroxy-2-phenylethyl)-2-dibenzofuranyl]-1-oxopentyl]), Rhone-Poulenc Rorer RP 66153 (2-Thiopheneheptanoic acid, .alpha.,.alpha.-dimethyl-3-(3-phenylpropyl)), SmithKline Beecham SB-201146 (2-Propenoic acid, 3-[6-[[[(3-aminophenyl)sulfinyl]methyl]-3-[[8-(4-methoxyphenyl)octyl]oxy]-2-pyridinyl]-, (2E)), SmithKline Beecham SB-201993 (Benzoic acid, 3-[[[[6-[(1E)-2-carboxyethenyl]-5-[[8-(4-methoxyphenyl)octyl]oxy]-2-pyridinyl]methyl]thio]methyl]), Searle SC-53228 (2H-1-Benzopyran-2-propanoic acid, 7-[3-[2-(cyclopropylmethyl)-3-methoxy-4-[(methylamino)carbonyl]phenoxy]propoxy]-3,4-dihydro-8-propyl-, (2S)), Sumitamo SM 15178 (.beta.-Alanine, N-[[6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]-2-pyridinyl]carbonyl]-N-ethyl),

and American Home Products WAY 121006 ([1,1'-Biphenyl]-4-acetic acid, 2-fluoro-4'-(2-quinolinylmethoxy)).--

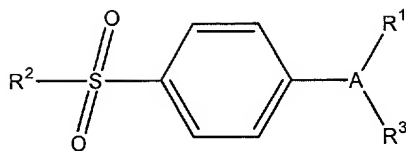
Please replace the paragraph on page 9, lines 16-19 with the following:

--Even more preferred leukotriene B₄ receptor antagonists include Bayer Bay-x-1005 ((R)-a-Cyclopentyl-4-(2-quinolinylmethoxy)benzeneacetic acid), Ciba-Geigy CGS-25019C (Benzamide, 4-[[5-[4-(aminoiminomethyl)phenoxy]pentyl]oxy]-3-methoxy-N,N-bis(1-methylethyl)-, (2Z)-2-butenedioate), ebselen (1,2-Benzisoselenazol-3(2H)-one, 2-phenyl), Leo Denmark ETH-615 (Benzoic acid, 4-[[[(3-fluorophenyl)methyl][4-(2-quinolinylmethoxy)phenyl]amino]methyl]), Lilly LY-293111 (Benzoic acid, 2-[3-[3-[(5-ethyl-4'-fluoro-2-hydroxy[1,1'-biphenyl]-4-yl)oxy]propoxy]-2-propylphenoxy]), Ono ONO-4057 (Benzenepropanoic acid, 2-(4-carboxybutoxy)-6-[[5E)-6-(4-methoxyphenyl)-5-hexenyl]oxy]), and Terumo TMK-688 (Carbonic acid, 4-[5-[2-[4-(diphenylmethoxy)-1-piperidinyl]ethyl]amino]-5-oxo-1,3-pentadienyl]-2-methoxyphenyl ethyl ester).--

IN THE CLAIMS:

Please replace Claim 2 with the following:

2. (once amended) A combination comprising a therapeutically-effective amount of a leukotriene B₄ receptor antagonist and a cyclooxygenase-2 inhibitor selected from Taisho NS-398 (Methanesulfonamide, N-[2-(cyclohexyloxy)-4-nitrophenyl]), meloxicam (2H-1,2-Benzothiazine-3-carboxamide, 4-hydroxy-2-methyl-N-(5-methyl-2-thiazolyl)-, 1,1-dioxide), flosulide (Methanesulfonamide, N-[6-(2,4-difluorophenoxy)-2,3-dihydro-1-oxo-1H-inden-5-yl]), Merck MK-966 (2(5H)-Furanone, 4-[4-(methylsulfonyl)phenyl]-3-phenyl), Merck L-752,860 and compounds of Formula I



wherein A is a substituent selected from partially unsaturated or unsaturated heterocyclyl and partially unsaturated or unsaturated carbocyclic rings;

wherein R¹ is at least one substituent selected from heterocyclyl, cycloalkyl, cycloalkenyl and aryl, wherein R¹ is optionally substituted at a substitutable position with one or more radicals selected from alkyl, haloalkyl, cyano, carboxyl, alkoxycarbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, arylamino, nitro, alkoxyalkyl, alkylsulfinyl, halo, alkoxy and alkylthio;

wherein R² is methyl or amino; and

wherein R³ is a radical selected from hydrido, halo, alkyl, alkenyl, alkynyl, oxo, cyano, carboxyl, cyanoalkyl, heterocyclyloxy, alkyloxy, alkylthio, alkylcarbonyl, cycloalkenyl, aralkyl, heterocyclylalkyl, acyl, alkylthioalkyl, hydroxyalkyl, alkoxycarbonyl, arylcarbonyl, aralkylcarbonyl, aralkenyl, alkoxyalkyl, arylthioalkyl, aryloxyalkyl, aralkylthioalkyl, aralkoxyalkyl, alkoxyaralkoxyalkyl, alkoxycarbonylalkyl, aminocarbonyl, aminocarbonylalkyl, alkylaminocarbonyl, N-arylaminocarbonyl, N-alkyl-N-arylaminocarbonyl, alkylaminocarbonylalkyl, carboxyalkyl, alkylamino, N-arylamino, N-aralkylamino, N-alkyl-N-aralkylamino, N-alkyl-N-arylamino, aminoalkyl, alkylaminoalkyl, N-arylaminalkyl, N-aralkylaminalkyl, N-alkyl-N-aralkylaminalkyl, N-alkyl-N-arylaminalkyl, aryloxy, aralkoxy, arylthio, aralkylthio, alkylsulfinyl, alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, N-arylaminosulfonyl, arylsulfonyl, N-alkyl-N-arylaminosulfonyl;

or a pharmaceutically-acceptable salt thereof.

Please replace Claim 3 with the following:

3. (once amended) The combination of Claim 2 wherein the leukotriene B₄ receptor antagonist is selected from Bayer Bay-x-1005 ((R)-a-Cyclopentyl-4-(2-quinolinylmethoxy) benzene acetic acid), Ciba-Geigy CGS-25019C (Benzamide, 4-[[5-[4-(aminoiminomethyl)phenoxy]pentyl]oxy]-3-methoxy-N,N-bis(1-methylethyl)-, (2Z)-2-butenedioate), ebselen (1,2-Benzisoselenazol-3(2H)-one, 2-phenyl), Leo Denmark ETH-615 (Benzoic acid, 4-[[[(3-fluorophenyl)methyl][4-(2-quinolinylmethoxy)phenyl]amino]methyl]), Lilly LY-293111 (Benzoic acid, 2-[3-[3-[(5-ethyl-4'-fluoro-2-hydroxy[1,1'-biphenyl]-4-yl)oxy]propoxy]-2-propylphenoxy]), Ono ONO-4057 (Benzenepropanoic acid, 2-(4-carboxybutoxy)-6-[[5E)-6-(4-methoxyphenyl)-5-hexenyl]oxy]), Terumo TMK-688 (Carbonic acid, 4-[5-[[2-[4-(diphenylmethoxy)-1-piperidinyl]ethyl]amino]-5-oxo-1,3-pentadienyl]-2-methoxyphenyl ethyl ester), Boehringer Ingleheim BI-RM-270 (2-Benzoxazamine, N-[(1S)-2-cyclohexyl-1-(2-pyridinyl)ethyl]-5-methyl), Lilly LY 213024 (Benzenepropanoic acid, 5-(3-carboxybenzoyl)-2-(decyloxy)), Lilly LY 264086 (9H-Xanthene-4-propanoic acid, 7-carboxy-3-(decyloxy)-9-oxo), Lilly LY 292728, Ono ONO LB457 (Benzenepropanoic acid, 2-(4-carboxybutoxy)-6-[[5E)-6-(4-methoxyphenyl)-5-hexenyl]oxy]), Pfizer 105696, Perdue Frederick PF 10042 (Pyrrolidine, 1-[5-hydroxy-5-[8-(1-hydroxy-2-phenylethyl)-2-dibenzofuranyl]-1-oxopentyl]), Rhone-Poulenc Rorer RP 66153 (2-Thiopheneheptanoic acid, .alpha.,.alpha.-dimethyl-3-(3-phenylpropyl)), SmithKline Beecham SB-201146 (2-Propenoic acid, 3-[6-[[3-(aminophenyl)sulfinyl]methyl]-3-[[8-(4-methoxyphenyl)octyl]oxy]-2-pyridinyl]-, (2E)), SmithKline Beecham SB-201993 (Benzoic acid, 3-[[[6-[(1E)-2-carboxyethenyl]-5-[[8-(4-methoxyphenyl)octyl]oxy]-2-pyridinyl]methyl]thio]methyl]), Searle SC-53228 (2H-1-Benzopyran-2-propanoic acid, 7-[3-[2-(cyclopropylmethyl)-3-methoxy-4-[(methylamino)carbonyl]phenoxy]propoxy]-3,4-dihydro-8-propyl-, (2S)), Sumitamo SM 15178 (.beta.-Alanine, N-[[6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]-2-pyridinyl]carbonyl]-N-ethyl),

American Home Products WAY 121006 ([1,1'-Biphenyl]-4-acetic acid, 2-fluoro-4'-(2-quinolinylmethoxy)), Bayer Bay-o-8276, calcitriol (9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, (1.alpha.,3.beta.,5Z,7E)), Warner-Lambert CI-987 (2,4-Thiazolidinedione,5-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]methylene]), Merck and Co. L-651392 (3H-Phenothiazin-3-one, 4-bromo-2,7-dimethoxy), Lilly LY 210073, Lilly LY 223982 (Benzenepropanoic acid, 5-(3-carboxybenzoyl)-2-[[5E)-6-(4-methoxyphenyl)-5-hexenyl]oxy]), Lilly LY-233569 (2-Propenamide, N-hydroxy-N-methyl-3-[2-(methylthio)phenyl]), Lilly LY-255283 (Ethanone, 1-[5-ethyl-2-hydroxy-4-[[6-methyl-6-(1H-tetrazol-5-yl)heptyl]oxy]phenyl]), Merck and Co. MK-591 (1H-Indole-2-propanoic acid, 1-[(4-chlorophenyl)methyl]-3-[(1,1-dimethylethyl)thio]-a,a-dimethyl-5-(2-quinolinylmethoxy)-, sodium salt), Merck and CO. MK-886 (1H-indole-2-propanoic acid, 1-[(4-chlorophenyl)methyl]-3-[(1,1-dimethylethyl)thio]-a,a-dimethyl-5-(1-methylethyl)), Ono ONO-LB-448, Purdue Frederick PF-5901 (Benzenemethanol, a-pentyl-3-(2-quinolinylmethoxy)), Rhone-Poulenc Rorer RG 14893 (2-Naphthalenecarboxylic acid, 4-[2-[methyl(2-phenylethyl)amino]-2-oxoethyl]-8-(phenylmethoxy)), Rhone-Poulenc Rorer RP 66364, Rhone-Poulenc Rorer RP 69698 (Pyridine, 2-[[5-methyl-5-(1H-tetrazol-5-yl)hexyl]oxy]-4,6-diphenyl), Searle SC-41930 (2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl), Searle SC-50505, Searle SC-51146, SmithKline Beecham SK&F-104493 (5H-Pyrrolo[1,2-a]imidazole, 6,7-dihydro-2-(4-methoxyphenyl)-3-(4-pyridinyl)), and Teinjin TEI-1338 (Benzoic acid, 2-[[4-[2-[2-(2-naphthalenyl)ethenyl]cyclopropyl]-1-oxobutyl]amino]-, methyl ester, [1R-[1.alpha.,2.beta.(E)]]).

Please replace Claim 4 with the following:

4. (once amended) The combination of Claim 3 wherein the leukotriene B₄ receptor antagonist is selected from Bayer Bay-x-1005 ((R)-a-Cyclopentyl-4-(2-quinolinylmethoxy)benzeneacetic acid), Ciba-Geigy CGS-25019C (Benzamide, 4-[[5-[4-(aminoiminomethyl)phenoxy]pentyl]oxy]-3-methoxy-N,N-bis(1-

methylethyl)-, (2Z)-2-butenedioate), ebselen (1,2-Benzisoselenazol-3(2H)-one, 2-phenyl), Leo Denmark ETH-615 (Benzoic acid, 4-[[[(3-fluorophenyl)methyl][4-(2-quinolinylmethoxy)phenyl]amino]methyl]), Lilly LY-293111 (Benzoic acid, 2-[3-[3-[(5-ethyl-4'-fluoro-2-hydroxy[1,1'-biphenyl]-4-yl)oxy]propoxy]-2-propylphenoxy]), Ono ONO-4057 (Benzenepropanoic acid, 2-(4-carboxybutoxy)-6-[[[(5E)-6-(4-methoxyphenyl)-5-hexenyl]oxy]), Terumo TMK-688 (Carbonic acid, 4-[5-[[2-[4-(diphenylmethoxy)-1-piperidinyl]ethyl]amino]-5-oxo-1,3-pentadienyl]-2-methoxyphenyl ethyl ester), Boehringer Ingelheim BI-RM-270 (2-Benzoxazamine, N-[(1S)-2-cyclohexyl-1-(2-pyridinyl)ethyl]-5-methyl), Lilly LY 213024 (Benzenepropanoic acid, 5-(3-carboxybenzoyl)-2-(decyloxy)), Lilly LY 264086 (9H-Xanthene-4-propanoic acid, 7-carboxy-3-(decyloxy)-9-oxo), Lilly LY 292728, Ono ONO LB457 (Benzenepropanoic acid, 2-(4-carboxybutoxy)-6-[[[(5E)-6-(4-methoxyphenyl)-5-hexenyl]oxy]), Pfizer 105696, Perdue Frederick PF 10042 (Pyrrolidine, 1-[5-hydroxy-5-[8-(1-hydroxy-2-phenylethyl)-2-dibenzofuranyl]-1-oxopentyl]), Rhone-Poulenc Rorer RP 66153 (2-Thiopheneheptanoic acid, .alpha.,.alpha.-dimethyl-3-(3-phenylpropyl)), SmithKline Beecham SB-201146 (2-Propenoic acid, 3-[6-[[[(3-aminophenyl)sulfinyl]methyl]-3-[[8-(4-methoxyphenyl)octyl]oxy]-2-pyridinyl]-, (2E)), SmithKline Beecham SB-201993 (Benzoic acid, 3-[[[[6-[(1E)-2-carboxyethenyl]-5-[[8-(4-methoxyphenyl)octyl]oxy]-2-pyridinyl]methyl]thio]methyl]), Searle SC-53228 (2H-1-Benzopyran-2-propanoic acid, 7-[3-[2-(cyclopropylmethyl)-3-methoxy-4-[(methylamino)carbonyl]phenoxy]propoxy]-3,4-dihydro-8-propyl-, (2S)), Sumitamo SM 15178 (.beta.-Alanine, N-[[6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]-2-pyridinyl]carbonyl]-N-ethyl), and American Home Products WAY 121006 ([1,1'-Biphenyl]-4-acetic acid, 2-fluoro-4'-(2-quinolinylmethoxy)).

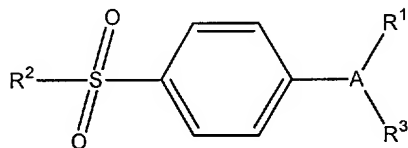
Please replace Claim 5 with the following:

5. (once amended) The combination of Claim 4 wherein the leukotriene B₄ receptor antagonist is selected from Bayer Bay-x-

1005 ((R)-a-Cyclopentyl-4-(2-quinolinylmethoxy)benzeneacetic acid), Ciba-Geigy CGS-25019C (Benzamide, 4-[[5-[4-(aminoiminomethyl)phenoxy]pentyl]oxy]-3-methoxy-N,N-bis(1-methylethyl)-, (2Z)-2-butenedioate), ebselen (1,2-Benzisoselenazol-3(2H)-one, 2-phenyl), Leo Denmark ETH-615 (Benzoic acid, 4-[[[(3-fluorophenyl)methyl][4-(2-quinolinylmethoxy)phenyl]amino]methyl]), Lilly LY-293111 (Benzoic acid, 2-[3-[3-[(5-ethyl-4'-fluoro-2-hydroxy[1,1'-biphenyl]-4-yl)oxy]propoxy]-2-propylphenoxy]), Ono ONO-4057 (Benzenepropanoic acid, 2-(4-carboxybutoxy)-6-[[5E)-6-(4-methoxyphenyl)-5-hexenyl]oxy]), and Terumo TMK-688 (Carbonic acid, 4-[5-[[2-[4-(diphenylmethoxy)-1-piperidinyl]ethyl]amino]-5-oxo-1,3-pentadienyl]-2-methoxyphenyl ethyl ester).

Please replace Claim 9 with the following:

9. (once amended) A pharmaceutical composition comprising a pharmaceutically-acceptable carrier and a therapeutically-effective amount of a leukotriene B₄ receptor antagonist and a cyclooxygenase-2 inhibitor selected from Taisho NS-398 (Methanesulfonamide, N-[2-(cyclohexyloxy)-4-nitrophenyl]), meloxicam (2H-1,2-Benzothiazine-3-carboxamide, 4-hydroxy-2-methyl-N-(5-methyl-2-thiazolyl)-, 1,1-dioxide), flosulide (Methanesulfonamide, N-[6-(2,4-difluorophenoxy)-2,3-dihydro-1-oxo-1H-inden-5-yl]), Merck MK-966 (2(5H)-Furanone, 4-[4-(methylsulfonyl)phenyl]-3-phenyl), Merck L-752,860 and compounds of Formula I



wherein A is a substituent selected from partially unsaturated or unsaturated heterocyclyl and partially unsaturated or unsaturated carbocyclic rings;

wherein R¹ is at least one substituent selected from heterocyclyl, cycloalkyl, cycloalkenyl and aryl, wherein R¹ is optionally substituted at a substitutable position with one or

more radicals selected from alkyl, haloalkyl, cyano, carboxyl, alkoxy carbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, arylamino, nitro, alkoxyalkyl, alkylsulfinyl, halo, alkoxy and alkylthio;

wherein R² is methyl or amino; and

wherein R³ is a radical selected from hydrido, halo, alkyl, alkenyl, alkynyl, oxo, cyano, carboxyl, cyanoalkyl, heterocycloxy, alkyloxy, alkylthio, alkylcarbonyl, cycloalkenyl, aralkyl, heterocyclylalkyl, acyl, alkylthioalkyl, hydroxyalkyl, alkoxy carbonyl, arylcarbonyl, aralkylcarbonyl, aralkenyl, alkoxyalkyl, arylthioalkyl, aryloxyalkyl, aralkylthioalkyl, aralkoxyalkyl, alkoxyaralkoxyalkyl, alkoxy carbonylalkyl, aminocarbonyl, aminocarbonylalkyl, alkylaminocarbonyl, N-arylaminocarbonyl, N-alkyl-N-arylaminocarbonyl, alkylaminocarbonylalkyl, carboxyalkyl, alkylamino, N-aryl amino, N-aralkyl amino, N-alkyl-N-aralkyl amino, N-alkyl-N-aryl amino, aminoalkyl, alkylaminoalkyl, N-aryl aminoalkyl, N-aralkyl aminoalkyl, N-alkyl-N-aralkyl aminoalkyl, N-alkyl-N-aryl aminoalkyl, aryloxy, aralkoxy, arylthio, aralkylthio, alkylsulfinyl, alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, N-arylaminosulfonyl, arylsulfonyl, N-alkyl-N-arylaminosulfonyl;

or a pharmaceutically-acceptable salt thereof.

Please cancel claims 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22 and 23.

[illegible][illegible]

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE RELATED CASE:

Please replace the paragraph on Page 1, lines 7-8 with the following:

--This is a continuation of US Application Serial No. 08/661,641, filed June 11, 1996 which application is a continuation-in-part of US Application Serial No. 08/489,415, filed June 12, 1995.--

IN THE SPECIFICATION:

Please replace the paragraph on page 5, lines 6-12 with the following:

--In addition, the invention describes a combination comprising a therapeutically-effective amount of a leukotriene B₄ receptor antagonist and a cyclooxygenase-2 inhibitor selected from Taisho NS-398 (Methanesulfonamide, N-[2-(cyclohexyloxy)-4-nitrophenyl]), meloxicam (2H-1,2-Benzothiazine-3-carboxamide, 4-hydroxy-2-methyl-N-(5-methyl-2-thiazolyl)-, 1,1-dioxide), [floculide] flosulide (Methanesulfonamide, N-[6-(2,4-difluorophenoxy)-2,3-dihydro-1-oxo-1H-inden-5-yl]), Merck MK-966 (2(5H)-Furanone, 4-[4-(methylsulfonyl)phenyl]-3-phenyl), Merck L-752,860 and compounds of Formula I--

Please replace the paragraph beginning on page 8, lines 26-37 and ending on page 9, lines 1-5 with the following:

--Preferred leukotriene B₄ receptor antagonists include Bayer Bay-x-1005 (((R)-a-Cyclopentyl-4-(2-quinolinylmethoxy) benzene acetic acid), Ciba-Geigy CGS-25019C (Benzamide, 4-[[5-[4-(aminoiminomethyl)phenoxy]pentyl]oxy]-3-methoxy-N,N-bis(1-methylethyl)-, (2Z)-2-butenedioate), ebselen (1,2-Benzisoselenazol-3(2H)-one, 2-phenyl), Leo Denmark ETH-615 (Benzoic acid, 4-[[[(3-fluorophenyl)methyl][4-(2-quinolinylmethoxy)phenyl]amino]methyl]), Lilly LY-293111 (Benzoic

acid, 2-[3-[3-[(5-ethyl-4'-fluoro-2-hydroxy[1,1'-biphenyl]-4-yl)oxy]propoxy]-2-propylphenoxy]], Ono ONO-4057 (Benzenepropanoic acid, 2-(4-carboxybutoxy)-6-[[(5E)-6-(4-methoxyphenyl)-5-hexenyl]oxy]], Terumo TMK-688 (Carbonic acid, 4-[5-[2-[4-(diphenylmethoxy)-1-piperidinyl]ethyl]amino]-5-oxo-1,3-pentadienyl]-2-methoxyphenyl ethyl ester), Boehringer Ingelheim BI-RM-270 (2-Benzoxazamine, N-[(1S)-2-cyclohexyl-1-(2-pyridinyl)ethyl]-5-methyl), Lilly LY 213024 (Benzenepropanoic acid, 5-(3-carboxybenzoyl)-2-(decyloxy)), Lilly LY 264086 (9H-Xanthene-4-propanoic acid, 7-carboxy-3-(decyloxy)-9-oxo), Lilly LY 292728, Ono ONO LB457 (Benzenepropanoic acid, 2-(4-carboxybutoxy)-6-[[(5E)-6-(4-methoxyphenyl)-5-hexenyl]oxy]], Pfizer 105696, Perdue Frederick PF 10042 (Pyrrolidine, 1-[5-hydroxy-5-[8-(1-hydroxy-2-phenylethyl)-2-dibenzofuranyl]-1-oxopentyl]], Rhone-Poulenc Rorer RP 66153 (2-Thiopheneheptanoic acid, .alpha.,.alpha.-dimethyl-3-(3-phenylpropyl)), SmithKline Beecham SB-201146 (2-Propenoic acid, 3-[6-[[(3-aminophenyl)sulfinyl]methyl]-3-[[8-(4-methoxyphenyl)octyl]oxy]-2-pyridinyl]-, (2E)), SmithKline Beecham SB-201993 (Benzoic acid, 3-[[[[6-[(1E)-2-carboxyethenyl]-5-[[8-(4-methoxyphenyl)octyl]oxy]-2-pyridinyl]methyl]thio]methyl]], Searle SC-53228 (2H-1-Benzopyran-2-propanoic acid, 7-[3-[2-(cyclopropylmethyl)-3-methoxy-4-[(methylamino)carbonyl]phenoxy]propoxy]-3,4-dihydro-8-propyl-, (2S)), Sumitamo SM 15178 (.beta.-Alanine, N-[[6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]-2-pyridinyl]carbonyl]-N-ethyl), American Home Products WAY 121006 ([1,1'-Biphenyl]-4-acetic acid, 2-fluoro-4'-(2-quinolinylmethoxy)), Bayer Bay-o-8276, calcitriol (9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, (1.alpha.,3.beta.,5Z,7E)), Warner-Lambert CI-987 (2,4-Thiazolidinedione,5-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]methylene]], Merck and Co. L-651392 (3H-Phenothiazin-3-one, 4-bromo-2,7-dimethoxy), Lilly LY 210073, Lilly LY 223982 (Benzenepropanoic acid, 5-(3-carboxybenzoyl)-2-[[(5E)-6-(4-methoxyphenyl)-5-hexenyl]oxy]], Lilly LY-233569 (2-Propenamide, N-hydroxy-N-methyl-3-[2-(methylthio)phenyl]], Lilly

LY-255283 (Ethanone, 1-[5-ethyl-2-hydroxy-4-[[6-methyl-6-(1H-tetrazol-5-yl)heptyl]oxy]phenyl]), Merck and Co. MK-591 (1H-Indole-2-propanoic acid, 1-[(4-chlorophenyl)methyl]-3-[(1,1-dimethylethyl)thio]-a,a-dimethyl-5-(2-quinolinylmethoxy)-, sodium salt), Merck and CO. MK-886 (1H-indole-2-propanoic acid, 1-[(4-chlorophenyl)methyl]-3-[(1,1-dimethylethyl)thio]-a,a-dimethyl-5-(1-methylethyl)), Ono ONO-LB-448, Purdue Frederick PF-5901 (Benzenemethanol, a-pentyl-3-(2-quinolinylmethoxy)), Rhone-Poulenc Rorer RG 14893 (2-Naphthalenecarboxylic acid, 4-[2-[methyl(2-phenylethyl)amino]-2-oxoethyl]-8-(phenylmethoxy)), Rhone-Poulenc Rorer RP 66364, Rhone-Poulenc Rorer RP 69698 (Pyridine, 2-[[5-methyl-5-(1H-tetrazol-5-yl)hexyl]oxy]-4,6-diphenyl), Searle SC-41930 (2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl), Searle SC-50505, Searle SC-51146, SmithKline Beecham SK&F-104493 (5H-Pyrrolo[1,2-a]imidazole, 6,7-dihydro-2-(4-methoxyphenyl)-3-(4-pyridinyl)), and Teinjin TEI-1338 (Benzoic acid, 2-[[4-[2-[2-(2-naphthalenyl)ethenyl]cyclopropyl]-1-oxobutyl]amino]-, methyl ester, [1R-[1.alpha.,2.beta.(E)]]).

Please replace the paragraph on page 9, lines 6-15 with the following:

--More preferred leukotriene B₄ receptor antagonists include Bayer Bay-x-1005 (((R)-a-Cyclopentyl-4-(2-quinolinylmethoxy)benzeneacetic acid), Ciba-Geigy CGS-25019C (Benzamide, 4-[[5-[4-(aminoiminomethyl)phenoxy]pentyl]oxy]-3-methoxy-N,N-bis(1-methylethyl)-, (2Z)-2-butenedioate), ebselen (1,2-Benzisoselenazol-3(2H)-one, 2-phenyl), Leo Denmark ETH-615 (Benzoic acid, 4-[[[(3-fluorophenyl)methyl][4-(2-quinolinylmethoxy)phenyl]amino]methyl]), Lilly LY-293111 (Benzoic acid, 2-[3-[3-[(5-ethyl-4'-fluoro-2-hydroxy[1,1'-biphenyl]-4-yl)oxy]propoxy]-2-propylphenoxy]), Ono ONO-4057 (Benzenepropanoic acid, 2-(4-carboxybutoxy)-6-[[[(5E)-6-(4-methoxyphenyl)-5-hexenyl]oxy]), Terumo TMK-688 (Carbonic acid, 4-[5-[2-[4-(diphenylmethoxy)-1-piperidinyl]ethyl]amino]-5-oxo-1,3-pentadienyl]-2-methoxyphenyl ethyl ester), Boehringer Ingleheim

BI-RM-270 (2-Benzoxazolamine, N-[(1S)-2-cyclohexyl-1-(2-pyridinyl)ethyl]-5-methyl), Lilly LY 213024 (Benzenepropanoic acid, 5-(3-carboxybenzoyl)-2-(decyloxy)), Lilly LY 264086 (9H-Xanthene-4-propanoic acid, 7-carboxy-3-(decyloxy)-9-oxo), Lilly LY 292728, Ono ONO LB457 (Benzenepropanoic acid, 2-(4-carboxybutoxy)-6-[[[(5E)-6-(4-methoxyphenyl)-5-hexenyl]oxy]), Pfizer 105696, Perdue Frederick PF 10042 (Pyrrolidine, 1-[5-hydroxy-5-[8-(1-hydroxy-2-phenylethyl)-2-dibenzofuranyl]-1-oxopentyl]), Rhone-Poulenc Rorer RP 66153 (2-Thiopheneheptanoic acid, .alpha.,.alpha.-dimethyl-3-(3-phenylpropyl)), SmithKline Beecham SB-201146 (2-Propenoic acid, 3-[6-[[[(3-aminophenyl)sulfinyl]methyl]-3-[[8-(4-methoxyphenyl)octyl]oxy]-2-pyridinyl]-, (2E)), SmithKline Beecham SB-201993 (Benzoic acid, 3-[[[6-[(1E)-2-carboxyethenyl]-5-[[8-(4-methoxyphenyl)octyl]oxy]-2-pyridinyl]methyl]thio]methyl]), Searle SC-53228 (2H-1-Benzopyran-2-propanoic acid, 7-[3-[2-(cyclopropylmethyl)-3-methoxy-4-[(methylamino)carbonyl]phenoxy]propoxy]-3,4-dihydro-8-propyl-, (2S)), Sumitamo SM 15178 (.beta.-Alanine, N-[[6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]-2-pyridinyl]carbonyl]-N-ethyl), and American Home Products WAY 121006 ([1,1'-Biphenyl]-4-acetic acid, 2-fluoro-4'-(2-quinolinylmethoxy)).--

Please replace the paragraph on page 9, lines 16-19 with the following:

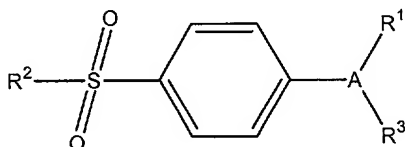
--Even more preferred leukotriene B₄ receptor antagonists include Bayer Bay-x-1005 ((R)-a-Cyclopentyl-4-(2-quinolinylmethoxy)benzeneacetic acid), Ciba-Geigy CGS-25019C (Benzamide, 4-[[5-[4-(aminoiminomethyl)phenoxy]pentyl]oxy]-3-methoxy-N,N-bis(1-methylethyl)-, (2Z)-2-butenedioate), ebselen (1,2-Benzisoselenazol-3(2H)-one, 2-phenyl), Leo Denmark ETH-615 (Benzoic acid, 4-[[[(3-fluorophenyl)methyl][4-(2-quinolinylmethoxy)phenyl]amino]methyl]), Lilly LY-293111 (Benzoic acid, 2-[3-[3-[(5-ethyl-4'-fluoro-2-hydroxy[1,1'-biphenyl]-4-yl)oxy]propoxy]-2-propylphenoxy]), Ono ONO-4057 (Benzenepropanoic acid, 2-(4-carboxybutoxy)-6-[[[(5E)-6-(4-methoxyphenyl)-5-

hexenyl]oxy]), and Terumo TMK-688 (Carbonic acid, 4-[5-[[2-[4-(diphenylmethoxy)-1-piperidinyl]ethyl]amino]-5-oxo-1,3-pentadienyl]-2-methoxyphenyl ethyl ester).--

IN THE CLAIMS:

CLAIM 2:

2. (once amended) A combination comprising a therapeutically-effective amount of a leukotriene B₄ receptor antagonist and a cyclooxygenase-2 inhibitor selected from Taisho NS-398 (Methanesulfonamide, N-[2-(cyclohexyloxy)-4-nitrophenyl]), meloxicam (2H-1,2-Benzothiazine-3-carboxamide, 4-hydroxy-2-methyl-N-(5-methyl-2-thiazolyl)-, 1,1-dioxide), [floculide] flosulide (Methanesulfonamide, N-[6-(2,4-difluorophenoxy)-2,3-dihydro-1-oxo-1H-inden-5-yl]), Merck MK-966 (2(5H)-Furanone, 4-[4-(methylsulfonyl)phenyl]-3-phenyl], Merck L-752,860 and compounds of Formula I



wherein A is a substituent selected from partially unsaturated or unsaturated heterocyclyl and partially unsaturated or unsaturated carbocyclic rings;

wherein R¹ is at least one substituent selected from heterocyclyl, cycloalkyl, cycloalkenyl and aryl, wherein R¹ is optionally substituted at a substitutable position with one or more radicals selected from alkyl, haloalkyl, cyano, carboxyl, alkoxy carbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, arylamino, nitro, alkoxyalkyl, alkylsulfinyl, halo, alkoxy and alkylthio;

wherein R² is methyl or amino; and

wherein R³ is a radical selected from hydrido, halo, alkyl, alkenyl, alkynyl, oxo, cyano, carboxyl, cyanoalkyl,

heterocyclyloxy, alkyloxy, alkylthio, alkylcarbonyl, cycloalkenyl, aralkyl, heterocyclylalkyl, acyl, alkylthioalkyl, hydroxyalkyl, alkoxycarbonyl, arylcarbonyl, aralkylcarbonyl, aralkenyl, alkoxyalkyl, arylthioalkyl, aryloxyalkyl, aralkylthioalkyl, aralkoxyalkyl, alkoxyaralkoxyalkyl, alkoxycarbonylalkyl, aminocarbonyl, aminocarbonylalkyl, alkylaminocarbonyl, N-arylaminocarbonyl, N-alkyl-N-arylaminocarbonyl, alkylaminocarbonylalkyl, carboxyalkyl, alkylamino, N-arylamino, N-aralkylamino, N-alkyl-N-aralkylamino, N-alkyl-N-arylamino, aminoalkyl, alkylaminoalkyl, N-arylaminoalkyl, N-aralkylaminoalkyl, N-alkyl-N-aralkylaminoalkyl, N-alkyl-N-arylaminoalkyl, aryloxy, aralkoxy, arylthio, aralkylthio, alkylsulfinyl, alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, N-arylaminosulfonyl, arylsulfonyl, N-alkyl-N-arylaminosulfonyl;

or a pharmaceutically-acceptable salt thereof.

CLAIM 3:

3. (once amended) The combination of Claim 2 wherein the leukotriene B₄ receptor antagonist is selected from Bayer Bay-x-1005 ((R)-a-Cyclopentyl-4-(2-quinolinylmethoxy) benzene acetic acid), Ciba-Geigy CGS-25019C (Benzamide, 4-[[5-[4-(aminoiminomethyl)phenoxy]pentyl]oxy]-3-methoxy-N,N-bis(1-methylethyl)-, (2Z)-2-butenedioate), ebselen (1,2-Benzisoselenazol-3(2H)-one, 2-phenyl), Leo Denmark ETH-615 (Benzoic acid, 4-[[[(3-fluorophenyl)methyl][4-(2-quinolinylmethoxy)phenyl]amino]methyl]]), Lilly LY-293111 (Benzoic acid, 2-[3-[3-[(5-ethyl-4'-fluoro-2-hydroxy[1,1'-biphenyl]-4-yl)oxy]propoxy]-2-propylphenoxy]), Ono ONO-4057 (Benzenepropanoic acid, 2-(4-carboxybutoxy)-6-[[5E)-6-(4-methoxyphenyl)-5-hexenyl]oxy]), Terumo TMK-688 (Carbonic acid, 4-[5-[[2-[4-(diphenylmethoxy)-1-piperidinyl]ethyl]amino]-5-oxo-1,3-pentadienyl]-2-methoxyphenyl ethyl ester), Boehringer Ingleheim BI-RM-270 (2-Benzoxazoline, N-[(1S)-2-cyclohexyl-1-(2-pyridinyl)ethyl]-5-methyl), Lilly LY 213024 (Benzenepropanoic acid, 5-(3-carboxybenzoyl)-2-(decyloxy)), Lilly LY 264086 (9H-

Xanthene-4-propanoic acid, 7-carboxy-3-(decyloxy)-9-oxo), Lilly LY 292728, Ono ONO LB457 (Benzenepropanoic acid, 2-(4-carboxybutoxy)-6-[[(5E)-6-(4-methoxyphenyl)-5-hexenyl]oxy]), Pfizer 105696, Perdue Frederick PF 10042 (Pyrrolidine, 1-[5-hydroxy-5-[8-(1-hydroxy-2-phenylethyl)-2-dibenzofuranyl]-1-oxopentyl]), Rhone-Poulenc Rorer RP 66153 (2-Thiopheneheptanoic acid, .alpha.,.alpha.-dimethyl-3-(3-phenylpropyl)), SmithKline Beecham SB-201146 (2-Propenoic acid, 3-[6-[[(3-aminophenyl)sulfinyl]methyl]-3-[[8-(4-methoxyphenyl)octyl]oxy]-2-pyridinyl]-, (2E)), SmithKline Beecham SB-201993 (Benzoic acid, 3-[[[6-[(1E)-2-carboxyethenyl]-5-[[8-(4-methoxyphenyl)octyl]oxy]-2-pyridinyl]methyl]thio]methyl]), Searle SC-53228 (2H-1-Benzopyran-2-propanoic acid, 7-[3-[2-(cyclopropylmethyl)-3-methoxy-4-[(methylamino)carbonyl]phenoxy]propoxy]-3,4-dihydro-8-propyl-, (2S)), Sumitamo SM 15178 (.beta.-Alanine, N-[[6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]-2-pyridinyl]carbonyl]-N-ethyl), American Home Products WAY 121006 ([1,1'-Biphenyl]-4-acetic acid, 2-fluoro-4'-(2-quinolinylmethoxy)), Bayer Bay-o-8276, calcitriol (9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, (1.alpha.,3.beta.,5Z,7E)), Warner-Lambert CI-987 (2,4-Thiazolidinedione,5-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]methylene]), Merck and Co. L-651392 (3H-Phenothiazin-3-one, 4-bromo-2,7-dimethoxy), Lilly LY 210073, Lilly LY 223982 (Benzenepropanoic acid, 5-(3-carboxybenzoyl)-2-[[(5E)-6-(4-methoxyphenyl)-5-hexenyl]oxy]), Lilly LY-233569 (2-Propenamide, N-hydroxy-N-methyl-3-[2-(methylthio)phenyl]), Lilly LY-255283 (Ethanone, 1-[5-ethyl-2-hydroxy-4-[[6-methyl-6-(1H-tetrazol-5-yl)heptyl]oxy]phenyl]), Merck and Co. MK-591 (1H-Indole-2-propanoic acid, 1-[(4-chlorophenyl)methyl]-3-[(1,1-dimethylethyl)thio]-a,a-dimethyl-5-(2-quinolinylmethoxy)-, sodium salt), Merck and CO. MK-886 (1H-indole-2-propanoic acid, 1-[(4-chlorophenyl)methyl]-3-[(1,1-dimethylethyl)thio]-a,a-dimethyl-5-(1-methylethyl)), Ono ONO-LB-448, Purdue Frederick PF-5901 (Benzenemethanol, a-pentyl-3-(2-quinolinylmethoxy)), Rhone-Poulenc Rorer RG 14893 (2-Naphthalenecarboxylic acid, 4-[2-

[methyl(2-phenylethyl)amino]-2-oxoethyl]-8-(phenylmethoxy)), Rhone-Poulenc Rorer RP 66364, Rhone-Poulenc Rorer RP 69698 (Pyridine, 2-[[5-methyl-5-(1H-tetrazol-5-yl)hexyl]oxy]-4,6-diphenyl), Searle SC-41930 (2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl), Searle SC-50505, Searle SC-51146, SmithKline Beecham SK&F-104493 (5H-Pyrrolo[1,2-a]imidazole, 6,7-dihydro-2-(4-methoxyphenyl)-3-(4-pyridinyl)), and Teinjin TEI-1338 (Benzoic acid, 2-[[4-[2-[2-(2-naphthalenyl)ethenyl]cyclopropyl]-1-oxobutyl]amino]-, methyl ester, [1R-[1.alpha.,2.beta.(E)]]].

CLAIM 4:

4. (once amended) The combination of Claim 3 wherein the leukotriene B₄ receptor antagonist is selected from Bayer Bay-x-1005 ((R)-a-Cyclopentyl-4-(2-quinolinylmethoxy)benzeneacetic acid), Ciba-Geigy CGS-25019C (Benzamide, 4-[[5-[4-(aminoiminomethyl)phenoxy]pentyl]oxy]-3-methoxy-N,N-bis(1-methylethyl)-, (2Z)-2-butenedioate), ebselen (1,2-Benzisoselenazol-3(2H)-one, 2-phenyl), Leo Denmark ETH-615 (Benzoic acid, 4-[[[(3-fluorophenyl)methyl][4-(2-quinolinylmethoxy)phenyl]amino]methyl]), Lilly LY-293111 (Benzoic acid, 2-[3-[3-[(5-ethyl-4'-fluoro-2-hydroxy[1,1'-biphenyl]-4-yl)oxy]propoxy]-2-propylphenoxy]), Ono ONO-4057 (Benzenepropanoic acid, 2-(4-carboxybutoxy)-6-[[5E)-6-(4-methoxyphenyl)-5-hexenyl]oxy]), Terumo TMK-688 (Carbonic acid, 4-[5-[2-[4-(diphenylmethoxy)-1-piperidinyl]ethyl]amino]-5-oxo-1,3-pentadienyl]-2-methoxyphenyl ethyl ester), Boehringer Ingelheim BI-RM-270 (2-Benzoxazoline, N-[(1S)-2-cyclohexyl-1-(2-pyridinyl)ethyl]-5-methyl), Lilly LY 213024 (Benzenepropanoic acid, 5-(3-carboxybenzoyl)-2-(decyloxy)), Lilly LY 264086 (9H-Xanthene-4-propanoic acid, 7-carboxy-3-(decyloxy)-9-oxo), Lilly LY 292728, Ono ONO LB457 (Benzenepropanoic acid, 2-(4-carboxybutoxy)-6-[[5E)-6-(4-methoxyphenyl)-5-hexenyl]oxy]), Pfizer 105696, Perdue Frederick PF 10042 (Pyrrolidine, 1-[5-hydroxy-5-[8-(1-hydroxy-2-phenylethyl)-2-dibenzofuranyl]-1-oxopentyl]), Rhone-Poulenc Rorer RP 66153 (2-Thiopheneheptanoic

acid, .alpha.,.alpha.-dimethyl-3-(3-phenylpropyl)), SmithKline Beecham SB-201146 (2-Propenoic acid, 3-[6-[[3-aminophenyl)sulfinyl]methyl]-3-[[8-(4-methoxyphenyl)octyl]oxy]-2-pyridinyl]-, (2E)), SmithKline Beecham SB-201993 (Benzoic acid, 3-[[[6-[(1E)-2-carboxyethenyl]-5-[[8-(4-methoxyphenyl)octyl]oxy]-2-pyridinyl]methyl]thio]methyl)), Searle SC-53228 (2H-1-Benzopyran-2-propanoic acid, 7-[3-[2-(cyclopropylmethyl)-3-methoxy-4-[(methylamino)carbonyl]phenoxy]propoxy]-3,4-dihydro-8-propyl-, (2S)), Sumitamo SM 15178 (.beta.-Alanine, N-[[6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]-2-pyridinyl]carbonyl]-N-ethyl), and American Home Products WAY 121006 ([1,1'-Biphenyl]-4-acetic acid, 2-fluoro-4'-(2-quinolinylmethoxy)).

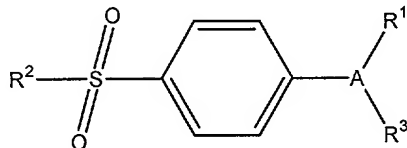
CLAIM 5:

5. (once amended) The combination of Claim 4 wherein the leukotriene B₄ receptor antagonist is selected from Bayer Bay-x-1005 ((R)-a-Cyclopentyl-4-(2-quinolinylmethoxy)benzeneacetic acid), Ciba-Geigy CGS-25019C (Benzamide, 4-[[5-[4-(aminoiminomethyl)phenoxy]pentyl]oxy]-3-methoxy-N,N-bis(1-methylethyl)-, (2Z)-2-butenedioate), ebselen (1,2-Benzisoselenazol-3(2H)-one, 2-phenyl), Leo Denmark ETH-615 (Benzoic acid, 4-[[[(3-fluorophenyl)methyl][4-(2-quinolinylmethoxy)phenyl]amino]methyl]), Lilly LY-293111 (Benzoic acid, 2-[3-[3-[(5-ethyl-4'-fluoro-2-hydroxy[1,1'-biphenyl]-4-yl)oxy]propoxy]-2-propylphenoxy]), Ono ONO-4057 (Benzenepropanoic acid, 2-(4-carboxybutoxy)-6-[[5-(4-methoxyphenyl)-5-hexenyl]oxy]), and Terumo TMK-688 (Carbonic acid, 4-[5-[[2-[4-(diphenylmethoxy)-1-piperidinyl]ethyl]amino]-5-oxo-1,3-pentadienyl]-2-methoxyphenyl ethyl ester).

CLAIM 9:

9. (once amended) A pharmaceutical composition comprising a pharmaceutically-acceptable carrier and a therapeutically-effective amount of a leukotriene B₄ receptor antagonist and a cyclooxygenase-2 inhibitor selected from Taisho NS-398

(Methanesulfonamide, N-[2-(cyclohexyloxy)-4-nitrophenyl]),
meloxicam (2H-1,2-Benzothiazine-3-carboxamide, 4-hydroxy-2-
methyl-N-(5-methyl-2-thiazolyl)-, 1,1-dioxide), [floculide]
flosulide (Methanesulfonamide, N-[6-(2,4-difluorophenoxy)-2,3-
dihydro-1-oxo-1H-inden-5-yl]), Merck MK-966 (2(5H)-Furanone, 4-
[4-(methylsulfonyl)phenyl]-3-phenyl), Merck L-752,860 and
compounds of Formula I



wherein A is a substituent selected from partially unsaturated or unsaturated heterocyclyl and partially unsaturated or unsaturated carbocyclic rings;

wherein R¹ is at least one substituent selected from heterocyclyl, cycloalkyl, cycloalkenyl and aryl, wherein R¹ is optionally substituted at a substitutable position with one or more radicals selected from alkyl, haloalkyl, cyano, carboxyl, alkoxycarbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, arylamino, nitro, alkoxyalkyl, alkylsufinyl, halo, alkoxy and alkylthio;

wherein R² is methyl or amino; and

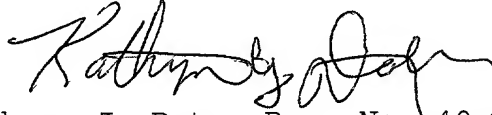
wherein R³ is a radical selected from hydrido, halo, alkyl, alkenyl, alkynyl, oxo, cyano, carboxyl, cyanoalkyl, heterocycliloxy, alkylloxy, alkylthio, alkylcarbonyl, cycloalkenyl, aralkyl, heterocyclylalkyl, acyl, alkylthioalkyl, hydroxyalkyl, alkoxycarbonyl, arylcarbonyl, aralkylcarbonyl, aralkenyl, alkoxyalkyl, arylthioalkyl, aryloxyalkyl, aralkylthioalkyl, aralkoxyalkyl, alkoxyaralkoxyalkyl, alkoxycarbonylalkyl, aminocarbonyl, aminocarbonylalkyl, alkylaminocarbonyl, N-arylaminocarbonyl, N-alkyl-N-arylaminocarbonyl, alkylaminocarbonylalkyl, carboxyalkyl, alkylamino, N-arylamino, N-aralkylamino, N-alkyl-N-aralkylamino, N-alkyl-N-arylamino, aminoalkyl, alkylaminoalkyl, N-arylaminalkyl, N-aralkylaminalkyl, N-alkyl-N-aralkylaminalkyl,

or a pharmaceutically-acceptable salt thereof.

Please cancel claims 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22 and 23.

If there are any additional charges in this matter, please
charge Deposit Account No. 19-1345.

Respectfully submitted,



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